

## I. AMENDMENTS

### IN THE CLAIMS

Please enter the amendments to claims 2 and 11, as shown below.

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31  
1. (Canceled)

2. (Currently Amended) A method for obtaining a mammalian cell comprising a genomic deletion in a range of from about 50 kb to about 3000 kb, which method comprises the steps of:

a) modifying the genome of mammalian cells comprising a wild-type target locus by introducing a construct comprising two regions of sequences that are homologous to the 5' and 3' flanking sequences of said wild-type target locus, wherein said homologous sequences are at least about 500 base pairs;

b) identifying cells containing said deletion by selecting cells containing a selectable marker present in said construct; and

c) recovering mammalian cell comprising said deletion.

3. (Previously Amended) The method of claim 2 wherein said target locus is an HPRT locus.

4. (Previously Amended) The method of claim 2 wherein said target locus is an MHC Class I locus.

5. (Previously Amended) The method of claim 2 wherein said target locus is an MHC Class II locus.

6. (Previously Amended) The method of claim 2 wherein said target locus is an immunoglobulin locus.

7. (Previously Amended) The method of claim 2 wherein said mammalian cell is selected from the group consisting of the islets of Langerhans, adrenal medulla cells, osteoblasts, osteoclasts, epithelial cells, endothelial cells, B lymphocytes, T lymphocytes, neurons, glial cells, ganglion cells, retinal cells, keratinocytes, embryonic stem (ES) cells, liver cells, bone marrow cells, and muscle cells.

8. (Withdrawn)

9.-10. (Canceled)

*Revised*

11. (Currently Amended) A method for preparing a mammalian cell deficient in hypoxanthine phosphoribosyltransferase (HPRT) HPRT, which method comprises introducing into target cells containing a wild-type HPRT locus a construct which comprises a modified DNA fragment, said fragment corresponding to the genomic site at which the wild-type HPRT locus is located, wherein said DNA fragment comprises a first sequence immediately downstream of the second exon of the *hprt* locus congruent with the wild-type sequence 55 kb upstream of said first sequence in the native DNA containing wild-type HPRT locus, wherein a mammalian cell deficient in HPRT is obtained.

12. (Original) The method of claim 11 which further comprises the steps of

- a) identifying cells containing said deletion by selecting cells containing a selectable marker present in said construct; and
- b) recovering cells containing said deletion.

13.-15. (Canceled)

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